The correlation between knee osteoarthritis and the ABO blood group system in a Turkish population

Knee osteoarthritis and the ABO blood group system

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Abstract

Aim: This study aimed to determine the validity of the relationship between primary knee osteoarthritis and the ABO blood group system in the Turkish population and whether ABO group system could be a risk factor for early-onset knee osteoarthritis or revision surgery.
Material and Methods: A retrospective examination of the data of 2752 patients who underwent knee arthroplasty surgery in our clinic between 2011 and 2019 was carried out. A total of 2436 primary knee osteoarthritis (PKO) patients underwent total knee arthroplasty (TKA) surgery and 206 patients underwent revision knee arthroplasty (RKA). A control group was formed of 22350 individuals aged >40 years from the same geographical region. The frequency of the ABO subgroups (A, B, O, AB) was compared between the primary knee osteoarthritis group and the control group. In addition, ABO subgroups (A, B, O, AB) were determined in the group of patients aged <65 with knee osteoarthritis (early-onset knee osteoarthritis) or revision group.
Results: In the PKO group, the female to male ratio was 8:1, and the mean age was 67.2±8 years. The most significant relationship between blood groups and osteoarthritis was found in Group A (p=0.001). Group AB had a significant but low relationship (p=0.002). However, no statistically significant difference was found between age <65 years and >65 years of age (p=0.642). In comparison with the PKO group and RKA, Group A in the revision group was seen at a statistically significantly higher rate (p=0.043).
Discussion: Group A blood group was found to be associated with both primary knee osteoarthritis and revision knee arthroplasty.

Keywords

Knee; Osteoarthritis; Blood group; Revision

Introduction

Osteoarthritis of the knee is a chronic degenerative disease with increasing prevalence with aging [1]. Osteoarthritis (OA) develops with the action of proinflammatory cytokines such as IL-1β and TNF-α, leading to a deterioration in chondrocyte metabolism [2, 3]. An increasing number of studies have reported the relationship between ABO blood group type and proinflammatory cytokines and the systemic inflammatory response [4].

The ABO blood group system, which is the most commonly used system in the classification of human blood, is based on hereditary features determined by the presence or absence of A and B antigens in red blood cells, tissue cells, saliva, and body fluids. The basis of the ABO blood group system was first defined by the Australian physician Landsteiner, and the Czech psychologist Janski, independently of each other in the first decade of the 20th century [5]. ABO antigens have been associated primarily with tumor disease, cerebrovascular and cardiovascular diseases, infection, and inflammatory diseases [6]. Previous studies have reported an association between blood groups and orthopaedic diseases such as musculoskeletal injuries and hip fractures [7,8]. These findings suggest that the genes and enzymes in the ABO system have pleiotropic roles.

A recent study by Li et al, conducted in Guangzhou city in China, is the only study in the literature to report the relationship between primary knee osteoarthritis (OA) and ABO blood groups. The study of a large patient sample included radiological grading and showed the frequency and severity of primary knee OA in ABO blood groups [9]. However, the frequency of ABO blood groups is known to be affected by many factors, and different frequencies are seen between communities and countries [10].

In knee arthroplasty, two patient groups are of importance: a) OA with onset at a young age and b) revision knee arthroplasty with major complications accompanying the inflammatory process. As Li et al. have stated that there could be a relationship between the ABO blood group system and gonarthrosis, naturally that there could be a relationship with early-onset OA or revision arthroplasty.

The aim of this study was to determine the validity of the relationship between the ABO blood group system and primary knee OA in the Turkish population and to investigate whether the ABO blood group system could constitute a risk for early knee OA or the need for revision surgery.

Material and Methods

Study design

A retrospective examination of the data of 2752 patients who underwent knee arthroplasty surgery in our clinic between 2011 and 2019 was carried out. After the exclusion of patients with inflammatory osteoarthritis, tumor disease, and age <40 years, a total of 2642 patients who underwent primary and revision surgery were included in the study. A total of 2436 patients evaluated as grade 3 and 4 according to Kellgren and Lawrencegrading system with persistent complaints of pain despite conservative treatment underwent primary knee arthroplasty surgery. Revision knee arthroplasty (RKA) was applied to 206 patients and the revision burden was determined as 7.4%. The control group was a representative subset of the

local population, aged >40 years from the same geographical area. The ABO blood group types were determined at the Blood Centre of the Başkent University Hospital. Approval for the study was granted by the Başkent University Hospital and all study procedures were performed in accordance with the ethical standards laid down in the Declaration of Helsinki. The ethics committee approval was obtained by the University of Health Sciences of Turkey affiliated hospital of Keçiören HPRC with the following 59. meeting on 15.05.2020, reference number: 43278876-929.

Determination of the ABO blood group

The ABO blood groups were tested using the standard agglutination method. The ABO blood group test is routine for patients of surgical departments, and is also performed for patients from other departments when needed. The determination of the ABO blood group types for the patient group in the study was performed in the clinical laboratory of Keçiören Health Practice and Research Hospital Blood Centre and for the control group in the Başkent University Hospital Blood Centre.

Knee osteoarthritis and ABO group

The frequencies of the ABO subgroups (A, B, O, AB) were compared between the primary knee osteoarthritis (PKO) group (n:2436) and the control group (n:22350), and risk groups for knee OA were investigated. The relationship with age and gender was determined with regression analysis. The PKO group was separated into two age groups as <65 years (n:1092) and > 65 years (n:1340) to determine the early onset of OA. The groups were compared to determine the relationship between ABO subtype and early onset OA. The details of the patient groups are shown in Figure 1.

Revision surgery and variables

Risk factors for revision surgery were determined as age, gender, comorbidity, and ABO blood group. To determine the relationship between the ABO blood group system and revision surgery, the ABO subtypes were compared between the PKO and RKA groups. To determine the relationship between septic revision and the ABO blood group system, the ABO subtypes were compared between the RKA septic cases and the RKA non-septic cases. Other risk factors for revision surgery that were investigated were determined as age, gender and comorbidity. The number of comorbidities was determined. The PKO and RKA groups were compared in respect of age, gender, and comorbidities.

Statistical analysis

Data obtained in the study were analyzed statistically using SPSS v.22 software with a 95% confidence interval. Qualitative data were stated as frequency distribution, and quantitative data were stated as mean, minimum, and maximum values. The x2 test was applied to categorical data, and the Student's t-test was applied to quantitative data. Normality of data distribution was tested with the Shapiro-Wilk test. Inter- and intra-observer reliability was assessed using the interclass coefficient. The PKO group and control group were compared in respect of the ABO blood group system using logistic regression analysis. The age and comorbidity values of the patients in the PKO and RKA groups were evaluated with the Mann-Whitney U test. Gender and ABO blood group types of the PKO and RKA groups were

compared using the Chi-square test. A value of p<0.05 was accepted as statistically significant.

Results

Demographic data of the patients and the control group

The primary knee osteoarthritis (PKO) group comprised 2436 patients with a gender ratio (F:M)- of 8:1, and a mean age of 67.2±8 years (range, 43-88 years). The control group comprised 22350 individuals with a gender ratio (F:M) of 1.2:1, and mean age of 57.4±10.36 years (range, 40-98 years). The Mann-Whitney U test showed that the mean age of the PKO group was statistically significantly older (p<0.001). As a result of the Chi-square test, the rate of female gender was determined to be statistically significantly higher in the PKO group (p<0.001) (Table 1).

Primary knee osteoarthritis and ABO subtype

In the PKO group, the blood group distribution was as follows: Group A: 1092 (44.8%), Group B: 404 (16.6%), Group O: 762 (31.3%) and Group AB: 176 (7.2%). In the control group, the blood group distribution was as follows: Group A: 9668 (43.2%), Group B: 3890 (17%), Group O: 6705 (30.4%) and Group AB: 2080 (9%) (Figure 2). The difference between the ABO subtypes was determined to be statistically significant (p=0.000). As a result of logistic regression analysis, the frequency of blood group A was determined to be high and group AB was low (A: p=0.001, B: p=0.145, O: p=0.345, AB: p=0.002). No statistically significant difference was determined between the two age subgroups of the PKO group (p=0.642) (Figure 3).

Table 1. Demographic data of the patients

	Primary Knee osteoarthritis	Control group	P value
Patients / Cases	2436	22350	
Age (years)	67.2 (43-88)	57.4 (40-98)	<0.001
Gender (F/M)	2174/260	12360/9990	<0.001
Number of comorbidities	2.3		

Table 2. Distribution of ABO blood groups in the primary knee osteoarthritis and revision knee arthroplasty groups.

ABO blood groups	A	B	O	AB	
Primary knee osteoarthritis	44.8	16.6	31.2	7.2	0.043
Revision knee arthroplasty	51.7	15.6	28.3	3.9	
Septic (89)	51.7	16.9	25.8	5.6	0.644
Non-septic (116)	51.7	14.7	30.2	2.6	

Table 3. Comparison of the results of the current study and the results of other studies in Turkey on the ABO group system

| ABO group system	A	B	O	AB	P value
Kızılay (All turkish population)	42.5	15.8	33.7	8	
Ergün et al. (n:298000)	44.6	15.4	32.2	7.6	
Current study control group (n:22,350)	43.2	17	30.4	9	0.000
Currrent study primary knee osteoarthritis group (2462)	44.8	16.6	31.2	7.2	

Revision knee arthroplasty and ABO subtype

In the revision group of 206 patients, the ABO subtypes were as follows: Group A: 107 (51.7%), Group B: 32 (15.6%), Group O: 59 (28.3%) and Group AB:8 (3.9%). In comparison with the PKO group, Group A in the revision group was seen at a statistically significantly higher rate (p=0.043) (Table 2). The RKA group was separated as septic (n:89, 43%) and non-septic (n:116, 57%) cases, and no significant difference was observed between the groups in respect of the ABO blood group types (p=0.644) (Table 2).

### Revision knee arthroplasty and risk factors

The RKA group comprised of 182 females and 24 males with a mean age of 71.1 years (range, 42-93 years). In comparison with the PKO group, a statistically significant difference was observed in respect of mean age (p<0.05), and the gender distribution was similar to the higher rate of females (p=0.746). The mean number of comorbidities was 3.2±1.3, which is significantly higher than in the PKO group (p=0.000). Age and comorbidity were determined to be risk factors for revision surgery.
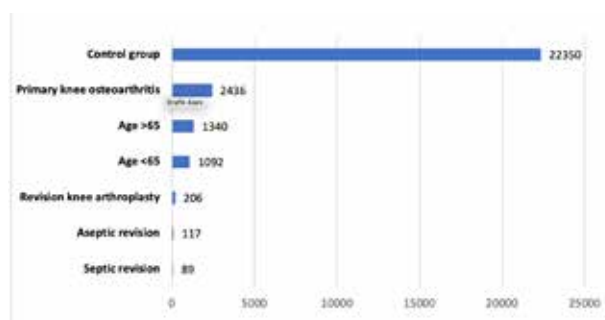
Figure 1. Data of study design
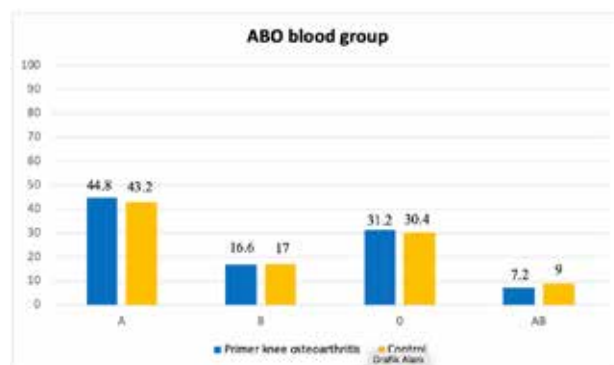
Figure 2. The relationship between the primary knee osteoarthritis group and the control group and the ABO blood group system
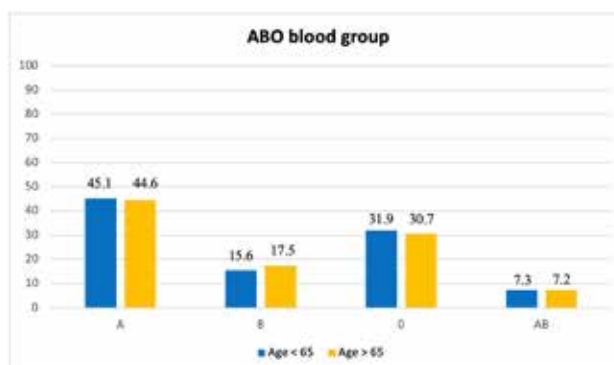
Figure 3. The relationship between early-onset knee osteoarthritis and the ABO blood group system

Discussion

The outcomes of this study demonstrated that blood group A is seen at a higher rate and Group AB is seen lower rate in PKO in the Turkish population in the comparison of ABO blood group distribution in the PKO group and the control group. There was also seen to be a significant difference in the ABO blood group distribution between the PKO group and the RKA group with blood group A seen at a higher rate in the revision group.

ABO blood group type has been associated with several diseases for osteoarthritis and primarily with abdominal cancers and cardiovascular diseases [5]. In 1975, Lourie et al. evaluated the association between ABO blood group and primary hip OA in a retrospective case-control study. Compared with the control group, the proportion of patients with blood group O was lower in the case group [11].

In a more specific group of patients with femoral head avascular necrosis (AVN), Yang et al. examined the relationship with ABO blood group [12]. Since it is known that there is a relationship between the ABO blood group type and venous thrombus diseases, Yang et al. focussed on the relationship with AVN [13]. Although no direct relationship was determined between AVN and ABO blood group, a more rapid progression of AVN in patients with blood group A was seen. Interestingly, there are different studies in the literature that have examined the association of ABO blood groups with orthopedic pathologies such as Achilles tendon rupture and rotator cuff arthropathy [14, 15].

Primary knee OA is a multifactorial disorder associated with the same factors such as age, female gender, obesity, osteoporosis, hypermobility, and hyperuricemia [2]. The only study in the literature related to primary knee OA and ABO blood groups was published in 2019 by Li et al. Although a statistically significant difference was observed in knee OA in the AB blood group, it was also noted that there was no significant difference between the patient and control groups in respect of the frequency of AB blood group (patient group: 9.7% AB, control group:7.8% AB). In the current study, as in the Li et al.'s study, a relationship was found between ABO blood groups and primary knee OA. Although the most important finding was that blood group A was associated with knee OA, it was also determined that blood group AB was seen less in the knee OA group (patient group: 44% group A, control group: 43.2% group A; patient group:7.2% group AB, control group: 9% AB). Based on this, it can be understood that the results of this study strengthen the relationship between OA and ABO blood groups, and it was concluded that differences may be seen between different populations. In the study by Li et al., although A B antigens in the joint synovium were not included in the histological section of the study, a close relationship was shown between H antigen and LeY antigen [8]. This histological finding also strengthens the hypothesis and results of both studies.

The distribution of blood groups shows variability between countries [9]. Group B is common in Asia, especially in southern India. Group A is common throughout the world but the highest incidence is seen in Australian Aborigines and Semitic races. In England, the blood group distribution of Groups A, B, O, and AB is 45%, 9%, 43% and 3%, respectively [9]. The Italian Blood Donation Association reported that the national distribution of Groups A, B, O, and AB is 32.02%, 14.10%, 50.63% and 3.25%, respectively [10]. Li et al. reported the Guangzhou Blood Centre control group to be 27.3% group A, 26.5% group B, 38.4% group O and 7.8% group AB [8]. The control group in the current study was determined as 43.2% group A, 17.4% group B, 30.2% group O, and 9% group AB. These results demonstrate that the relationship between blood group and disease must be evaluated at the community level.

Blood group A is common in the Turkish population. According to the data of 5 million people reported by the Turkish Red Crescent, blood group distribution is as follows: A: 42.5%, B:15.8%, O: 32.2%, and AB:7.6% [10]. In a study on 288,469 subjects by Ergün et al., conducted in a similar location to that of the current study, the blood group rates were found to be as follows: A: 44.62%, B: 15.45%, O: 32.24%, and AB: 7.69% [16]. The comparison of the study and control group of this study and two large groups of data are shown in Table 3. The fact that blood group A was most common in the PKO group of the current study shows consistency with the data of these other two studies. Previous studies in the literature have shown an association between blood group A and disease [17-19]. In studies determining the relationship between ABO blood groups and osteoporosis, with the exception of group O, a relationship has been shown with osteoporosis [17, 18].

In a study of hip fractures, Buckwalter et al. reported increased fracture incidence in the A blood group [19]. Kuru et al. also examined the relationship between hip fractures and ABO blood groups, and determined a relationship between extracapsular fractures and blood group A. In that study by Kuru et al., not only the relationship between disease and ABO blood groups, but also the relationship between the ABO group system and length of hospital stay and blood transfusion was examined [10].

Unlike other studies in the literature, significant differences were found in the revision arthroplasty group of the two groups that received a lot of attention in the current study (early-onset OA and revision arthroplasty). A new finding in the revision arthroplasty group was the significant relationship between revision surgery and blood group A (p=0.043). A relationship was found between the revision arthroplasty group and ABO blood groups, and risk factors were determined as age, comorbidities, and blood group A. It has been stated that the combination of the inflammatory process with septic revision is inevitable, but this situation may not be expected for non-septic patients. However, the study by Loria et al. changes this view as it showed that an increase in inflammatory cytokines within the joint in non-septic patients could cause inflammation in non-septic patients [20]. The combination of inflammatory symptoms with revision arthroplasty can be explained by the relationship of ABO blood groups with revision arthroplasty. Other risk factors for revision arthroplasty found in this study were age and comorbidities, which is consistent with the literature [21].

The other group of importance in the PKO group was the group with advanced OA determined at a young age. The early onset of PKO not only diminishes the quality of life of the patient at a young age but also leads to a severe treatment process. Genetic studies of OA at a young age have come to prominence. While some studies have reported that there may be a

relationship between OA and genomes (CALM 1), others have determined no relationship with genomes (ADAM12, GDF5) [22, 23]. Nevertheless, in genome studies, the relationship of genes and populations is mentioned. In the current study, while the distribution of ABO blood groups was similar in the younger patient group and those aged >65 years, the blood group was seen as a risk factor for the early onset of OA (p=0.664).

By keeping the number of participants high in both the patient and control groups in the current study, it was aimed to achieve high reliability of the results and to reduce the effects of the variables. A limitation of the study is the retrospective design and the fact that the details were taken from medical records. There is a need for further studies including more patients in the revision group and the support of a study including genetic patterns.

In conclusion, the results of our study determined a relationship between blood group A and both knee OA and revision knee arthroplasty. However, our study found a low relationship between the AB group and knee OA. Nevertheless, the relationship between the ABO blood group system and osteoarthritis can show variations between populations.

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